REMARKS

Claims 117-120 and 124-132 are pending in this application. Claims 130-132 have been withdrawn from prosecution as directed to non-elected subject matter. Claim 121-123 and 133-135 have been previously cancelled. Claims 117-120 and 124-132 have been objected to or stand rejected under 35 U.S.C. §§ 112, first paragraph; or § 103. Furthermore, the Examiner has objected to the specification. In view of the amendments and remarks below, Applicants respectfully request that the objections and rejections be reconsidered and withdrawn.

OBJECTION TO THE CLAIMS

Claims 124, 128 and 129 has been objected to because these claims contain a typographical error. Namely, claims 124 recites "polyoxyethylene phenyl ether X100" instead of "polyoxyethylene phenyl ether", and claims 128 and 129 recite "same" instead of "sample". Applicants have amended these claims to correct these typographical errors. Accordingly, withdrawal of these objections is respectfully requested.

REJECTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH

Claims 125, 128 and 129 have been rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement because these claims recite new matter. Specifically, the Examiner contends that the recitation of "mixing, homogenizing, adding, first washing, second washing, and resuspending steps are performed at a neutral pH" in claim 125 constitutes new matter. Claim 125 has been cancelled and claims 128 and 129 have been amended to depend from claim 117. Accordingly, withdrawal of this rejection is respectfully requested.

REJECTION UNDER 35 U.S.C. § 103

Claims 117-120 and 124-129 have been rejected under 35 U.S.C. § 103 in view of the following combination of references:

Claim(s)	Cited References
117-120 and 124-126	Chakravorty[1], Jaber[2] and Hernstadt[3]
127-129	Chakravorty, Jaber, Hernstadt, GenBank[4], Marchetti[5] and Buck[6]

Applicants respectfully traverse these rejections for the reasons set forth below.

I. REJECTION OF CLAIMS 117-120 AND 124-126

This invention, as recited in claim 117, is a method of processing clinical samples useful for diagnosis of bacterial infections. The method recites six solutions:

- Solution 1: a Universal Sample Processing (USP) solution comprising 3-6 M Guanidinium Hydrochloride (GuHC1), 40-60 mM Tris-Cl at a pH ranging between 7.3-7.7, 20-30 mM EDTA, 0.3-0.8% Sarcosyl, and 0.1-0.3 M beta-mercaptoethanol;
- Solution 2: 65 to 70 mM sodium phosphate at pH ranging between 6.7 to 6.8, or sterile water;
- Solution 3: 0.03 to 0.08% of polysorbate 80;
- Solution A: 8-12% a chelating resin;
- Solution B: 0.02 to 0.04% polyoxyethylene phenyl ether; and
- Solution C: 0.2-0.4% polysorbate 20.

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[1] Chakravorty *et al.*, "Novel use of guanidinium isothiocyanate in the isolation of *Mycobacterium tuberculosis* DNA from clinical material," FEMS MICROBIOLOGY LETTERS (2001) 205: 113-117 ("Chakravorty).

[2] Jaber *et al.*, "A simple method of DNA extraction from *Mycobacterium tuberculosis*," TUBERCLE AND LUNG DISEASE (1995) 76: 578-581 ("Jaber").

[3] United States Patent No. 6,027,883 to Herrnstadt *et al.* ("Herrnstadt").

[4] GenBank Accession No. U22037 ("GenBank").

[5] Marchetti *et al.*, "Evaluation of PCR in detection of *Mycobacterium tuberculosis* from formalin-fixed, paraffin-embedded tissues: comparison of four amplification assays," J. OF CLINICAL MICROBIOLOGY (1998) 36(6): 1512-1517 ("Marchetti").

[6] Buck *et al.*, ""Design strategies and performance of custom DNA sequencing primers," BIOTECHNIQUES (1999) 27(3): 528-536 ("Buck")

The method comprises obtaining the clinical sample. The clinical sample is mixed with 1.5 to 2 volumes of Solution 1. The clinical sample and Solution 1 are homogenized in a manner that avoids frothing. Solution 2 is added to the homogenate followed by centrifugation to obtain a pellet. The pellet is washed with Solution 1 and then optionally washed with water. The pellet is resuspended in one or more of Solutions 3, A, B and/or C to obtain a processed sample.

The purpose of processing with the USP solution is to lyse and remove all cells except the mycobacteria. The pellet obtained contains the viable mycobacteria and can be used in smear microscopy, to culture the mycobacteria and for DNA isolation.

In contrast, Chakravorty discusses a DNA isolation method.[7] The method consists of homogenizing a tissue in 5M GITC, 50mM Tris-CL, pH 7.5, 25 mM EDTA 0.5% Sarcosyl, 0.2 M β-mercaptoethanol, which Chakravorty refers to as an "inhibitor removal solution" or "IRS".[8] As the Examiner acknowledges, Chakravorty does not teach using GuHCl.

According to Chakravorty's method, once homogenized, the sample is centrifuged and the supernatant discarded.[9] The pellet is resuspended in the IRS, centrifuged, and the subsequent DNA-containing pellet is rinsed with water and dried.[10] Charkovarty's pellet does not contain viable mycobacteria.

Jaber is directed to a method of DNA extraction of *M. tuberculosis*.[11] Jaber's method consists of incubating a mycobacterium culture in a lysis buffer consisting of 6M guanidinium HCl, 50mM EDTA, 1 mM 2-mercaptoethanol and 0.05% Tween 80.[12] After the bacteria is incubated in the lysis buffer, the sample is centrifuged. The resulting supernatant, which contains the DNA is transferred into a clean tube, and the DNA is precipitated with

[7] Chakravorty at page 114.

[8] *Id.*

[9] *Id.*

[10] *Id.*

[11] Jaber at 578.

[12] *Id.* at 579.

cold ethanol.[13] Jaber's use of 6M guanidinium HCl leads to a loss of viability and inability to culture the mycobacteria.

As mentioned above, neither Chakravorty nor Jaber disclose isolating viable mycobacteria. Instead, they teach isolating DNA. When making a rejection under 35 U.S.C. § 103, the Examiner has the burden of establishing a *prima facie* case of obviousness. *In re Fritch*, 23 U.S.P.Q.2d 1780, 1783 (Fed. Cir. 1992). To establish a *prima facie* case of obviousness, the prior art must be evaluated based on what it, as a whole, teaches to one of ordinary skill in the art. *In re McLaughlin*, 443 F.2d 1392 (CCPA 1971).

Reviewing Chakravorty and Jaber as a whole, neither teaches nor suggests isolating viable mycobacteria. Moreover, a reason why one would expect that the recited USP would yield viable mycobacteria has not been provided. Accordingly, Applicants respectfully request that this rejection be reconsidered and withdrawn.

II. REJECTION OF CLAIMS 127-129

Claims 127-129, which directly or indirectly depend from claim 117, are patentable over these references for the same reason claim 117 is patentable over the combination of Chakravorty, Jaber and Herrnstadt.

OBJECTION TO THE SPECIFICATION

The Specification has been objected to because it contains an embedded hyperlink on page 61. Applicants have deleted this hyperlink from the Specification. Accordingly, withdrawal of this objection is respectfully requested.

[13] *Id.*

CONCLUSION

Accordingly, claim 117 is patentable over the cited references. Claims 118-120, 124 and 126-129 are also patentable over the cited references by virtue of their dependence on claim 117. Therefore, in view of the amendments to the claims and remarks, Applicants respectfully request that the objections and rejections asserted be reconsidered and withdrawn, that pending claims 117-120, 124 and 126-129 be allowed. The Applicants further request that claims 130-132 be rejoined and allowed.

Respectfully submitted,

THE WEBB LAW FIRM

By _____

William H. Logsdon
Registration No. 22,132
Attorney for Applicants
700 Koppers Building
436 Seventh Avenue
Pittsburgh, PA 15219
Telephone: (412) 471-8815
Facsimile: (412) 471-4094
E-mail: webblaw@webblaw.com